

bo) utilizing a force field calculation to generate a primary library of tayorably ranked primary variant proteins comprising a plurality of primary variant amino acid residues at primary variant positions; and

d) determining a criteria for selecting amino acid residues from each of said variant positions from said favorably ranked primary variant protoins

 e) selecting amino acid residues from a plurality of said variant positions from said favorably ranked primary variant proteins; and

of) computationally processing a plurality of said primary variant <u>solected amino acid residues</u> from a <u>plurality of said variant positions from said favorably ranked primary variant proteins etop b)</u>to generate a secondary library of secondary variant proteins.

35. (Currently amended) A method for generating a secondary library of <u>secondary</u> protein variants of a target protein comprising:

a) inputting the three dimensional coordinates of said target protein into a computer;

b) determining a criteria for including favorably ranked primary variant proteins for a primary

bg) utilizing a force_field calculation to generate a primary library of favorably ranked primary protein variants comprising a plurality of primary-variant amino acid residues at primary-variant positions;

d) determining a criteria for selecting amino acid residues from each of said variant positions from said favorably ranked primary variant proteins

e) selecting amino acid residues from a plurality of said variant positions from said favorably ranked primary variant proteins; and

ef) computationally processing a plurality of said primary-variant <u>selected</u> amino acid residues from <u>a plurality of said variant positions from said favorably ranked primary variant proteins</u> etep b)-to generate a secondary library of secondary variant proteins, wherein at least one of said secondary variant proteins is different from the <u>said primary variant proteins</u>.

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REMARKS

Claims 12, 13, 21-24 and 33-35 are pending. Support for the amended claims is found in the specification and the claims as originally filed. The amendment of the existing claims does not affect inventorship.

Claim Rejections - 35 USC §§ 101/112-1

4. Claims 12, 13, 21-24 and 33-35 are rejected under 35 USC §§ 101/112-1 because the claimed invention is not supported by either a specific asserted utility or a well-established utility. Applicants have amended the claims to require that the primary library be comprised of favorably ranked primary protein variants. Applicants believe this amendment clarifies that the pending claims have a specific utility. Applicants respectfully request that the rejection under 35 U.S.C. § 101/112-1 be withdrawn.

Claim Rejections - 35 USC § 112, second paragraph

5. Claims 12 and 35 are rejected under 35 USC § 112, second paragraph, as being indefinite for falling to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 12 and 35 have been amended to provide antecedent basis for the term "primary variant proteins". Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Claim Rejections - 35 USC §§ 102 and 103

6. Claims 12, 13, and 33-35 are rejected under 35 USC § 102(e) as being anticipated by Lacrolx et al. (US 2002/0072864; filing date 08/31/1999). All Independent claims in the application have been amended and Applicants respectfully submit that the claims, as amended, are not anticipated or made obvious by the references of record.

As amended, all pending claims require the generation of a secondary library by using several specific steps. As claimed, the secondary library is not "simply a collection of amino acid residues." The secondary library is a combination of selected amino acids at a plurality of variant positions from a plurality of favorably ranked primary variant proteins (i.e. proteins in the primary library). Without repeating the previously presented arguments in detail, Applicants respectfully submit that Lacroix does not teach or suggest the generation of a secondary library from information from a primary library, as required in all the pending claims. Rather, Lacroix teaches the generation of a list of variant proteins, and then the method can be run a second time to generate a different list of variant proteins. At best, this would be similar to two separate

primary libraries. Lacroix does not teach or suggest using selected amino acid residues at variant positions in a primary library to generate a secondary library, as required in the pending claims. Since Lacroix does not teach or suggest every limitation found in the amended claims, Applicants respectfully submit that Lacroix cannot anticipate the amended claims. Additionally, the other references of record do not teach or suggest the missing limitation and thus do not make the pending claims obvious. Applicants respectfully request that the rejections under 35 U.S.C. §§ 102 and 103 be withdrawn.

Double Patenting

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8. Claims 12 and 21-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19-29 of co-pending application no. 09/927790.

Applicant respectfully requests that the claim scope be reevaluated once the claims of both applications are in condition for allowance.

The Applicants submit that in light of the above-amendment and argument, the claims are now in condition for allowance and an early notification of such is respectfully solicited.

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